From the INTERNATIONAL BUREAU

PCT

NOTIFICATION OF TRANSMITTAL
OF COPIES OF TRANSLATION
OF THE INTERNATIONAL PRELIMINARY REPORT
ON PATENTABILITY
(CHAPTER I OR CHAPTER II
OF THE PATENT COOPERATION TREATY)
(PCT Rules 44*bis*.3(c) and 72.2)

To:

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Date of mailing *(day/month/year)* 01 March 2007 (01.03.2007)	
Applicant's or agent's file reference C1-A0407P	**IMPORTANT NOTIFICATION**
International application No. PCT/JP2005/007962	International filing date *(day/month/year)* 27 April 2005 (27.04.2005)
Applicant CHUGAI SEIYAKU KABUSHIKI KAISHA et al	

1. **Transmittal of the translation to the applicant.**

☐ The International Bureau transmits herewith a copy of the English translation of the international preliminary report on patentability (Chapter I).

☑ The International Bureau transmits herewith a copy of the English translation of the international preliminary report on patentability (Chapter II).

2. **Transmittal of the copy of the translation to the designated or elected Offices.**

The International Bureau notifies the applicant that copies of that translation have been transmitted to the following designated or elected Offices requiring such translation:

EP, KR

The following designated or elected Offices, having waived the requirement for such a transmittal at this time, will receive copies of that translation from the International Bureau only upon their request:

AE, AG, AL, AM, AP, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EA, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OA, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

3. **Reminder regarding translation into (one of) the official language(s) of the elected Office(s).**

The applicant is reminded that, where a translation of the international application must be furnished to an elected Office, that translation must contain a translation of any annexes to the international preliminary report on patentability (Chapter II).

It is the applicant's responsibility to prepare and furnish such translation directly to each elected Office concerned within the applicable time limit (Rule 74.1). See Volume II of the PCT Applicant's Guide for further details.

The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland	Authorized officer Masashi Honda

TRANSLATION

PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

(Chapter II of the Patent Cooperation Treaty)

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference	FOR FURTHER ACTION	See Form PCT/IPEA/416
C1-A0407P		
International application No	International filing date (*day/month/year*)	Priority date (*day/month/year*)
PCT/JP2005/007962	27.04.2005	27.04.2004

International Patent Classification (IPC) or national classification and IPC

C12N15/09(2006.01), A61K31/7088(2006.01), A61K35/12(2006.01), A61K39/395(2006.01), 61K48/00(2006.01), A61P31/12(2006.01), A61P35/00(2006.01), C07K16/32(2006.01), C12N5/02]2006.01), C12P21/08(2006.01), C12R1/91(2006.01)

Applicant

CHUGAI SEIYAKU KABUSHIKI KAISHA

1 This report is the international preliminary examination report, established by this International Preliminary Examining Authority under Article 35 and transmitted to the applicant according to Article 36

2 This REPORT consists of a total of _____ sheets, including this cover sheet

3 This report is also accompanied by ANNEXES, comprising:

a ☐ (*sent to the applicant and to the International Bureau*) a total of _____ sheets, as follows:

☐ sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications authorized by this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions)

☐ sheets which supersede earlier sheets, but which this Authority considers contain an amendment that goes beyond the disclosure in the international application as filed, as indicated in item 4 of Box No. I and the Supplemental Box.

b ☐ (*sent to the International Bureau only*) a total of (indicate type and number of electronic carrier(s))

_____, containing a sequence listing and/or tables related thereto, in computer readable form only, as indicated in the Supplemental Box Relating to Sequence Listing (see Section 802 of the Administrative Instructions).

4 This report contains indications relating to the following items:

☒ Box No. I Basis of the report

☐ Box No. II Priority

☐ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

☐ Box No. IV Lack of unity of invention

☒ Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

☐ Box No. VI Certain documents cited

☐ Box No. VII Certain defects in the international application

☐ Box No. VIII Certain observations on the international application

Date of submission of the demand	Date of completion of this report
Name and mailing address of the IPEA/JP	Authorized officer
Facsimile No.	Telephone No.

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International application No
PCT/JP2005/007962

Box No. I Basis of the report

1 With regard to the language, this report is based on the international application in the language in which it was filed, unless otherwise indicated under this item.

☐ This report is based on translations from the original language into the following _____, which is the language of a translation furnished for the purposes of:

☐ international search (Rule 12.3 and 23.1(b))

☐ publication of the international application (Rule 12.4)

☐ international preliminary examination (Rule 55.2 and/or 55.3)

2 With regard to the elements of the international application, this report is based on (*replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report*):

☒ the international application as originally filed/furnished

☐ the description:

pages _____ as originally filed/furnished

pages[1] _____ received by this Authority on _____

pages[1] _____ received by this Authority on _____

☐ the claims:

nos. _____ as originally filed/furnished

nos.[1] _____ as amended (together with any statement) under Article 19

nos.[1] _____ received by this Authority on _____

nos.[1] _____ received by this Authority on _____

☐ the drawings:

sheets _____ as originally filed/furnished

sheets[1] _____ received by this Authority on _____

sheets[1] _____ received by this Authority on _____

☒ a sequence listing and/or any related table(s) see Supplemental Box Relating to Sequence Listing

3 ☐ The amendments have resulted in the cancellation of:

☐ the description, pages _____

☐ the claims, nos. _____

☐ the drawings, sheets/figs _____

☐ the sequence listing (*specify*): _____

☐ any table(s) related to sequence listing (*specify*): _____

4 ☐ This report has been established as if (some of) the amendments annexed to this report and listed below had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).

☐ the description, pages _____

☐ the claims, nos. _____

☐ the drawings, sheets/figs _____

☐ the sequence listing (*specify*): _____

☐ any table(s) related to sequence listing (*specify*): _____

[1] *If item 4 applies, some or all of those sheets may be marked "superseded."*

Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1 Statement

Novelty (N)	Claims	3-33	YES
	Claims	1, 2	NO
Inventive step (IS)	Claims		YES
	Claims	1-33	NO
Industrial applicability (IA)	Claims	1-33	YES
	Claims		NO

2. Citations and explanations (Rule 70.7)

Cited document 1: Hitoshi KIYOI et al., "NOG Mouse eno Ishu Ishokukei o Mochiita Hito Saitaiketsu CD34 Yosei Saibo kara no B Saibo Bunka Katei no Kaiseki, Mukinseibutsu", 2003, Vol. 33, No. 2, p. 104-106

Cited document 2: Hideto KANASHIMA et al., "SCID-hu Mouse-Hito Zoketsu Menekikei Kenkyu eno Oyo, Taisha", 1990, Vol. 27, No. June, Special extra issue, p. 149-154

Cited document 3: Kazuo SHIMAMURA et al., "Hito Lymph-kyu no Shinseiji SCID Mouse eno Ishoku", Men'ekisei Shinkei Shikkan Chosa Kenkyuhan, Heisei 6 Nendo Kenkyu Hokokusho, Men'ekisei Shinkei Shikkan ni Kansuru Kenkyu, 1995, p. 106-108

Cited document 4: Depraetere S et al, Human B cell growth and differentiation in the spleen of immunodeficient mice., J. Immunol., 2001, Vol. 166, No. 5, p. 2929-2936

Cited document 5: Donze HH et al, Human and nonhuman primate lymphocytes engrafted into SCID mice reside in unique mesenteric lymphoid structures., J. Immunol., 1998, Vol. 161, No. 3, p. 1306-1312

Cited document 6: Norio UMEMOTO et al., "Jusho Fukugo Men'eki Fuzen (SCID) Mouse ni okeru Hito Men'eki Kiko Saikochiku ni Kansuru Kisoteki Kento", Biotherapy, 1991, Vol. 5, No. 3, p. 488-492

Cited document 7: Kubota T et al, High human IgG levels in severe combined immunodeficient mouse reconstituted with human splenic tissues from patients with gastric cancer., Jpn J Cancer Res., 1992, Vol. 83, No. 3, p. 300-303

Claim 1

Cited document 1 describes that a human cord blood CD34-positive cell is transplanted to an NOD/SCID/γcnull (NOG) mouse which is an immunodeficient mouse and that a plasma cell is observed after the transplantation (right column III2 of page 104 in cited document 1).

Cited document 2 describes that when a hematopoietic system or an immune system cell is transplanted to a severe combined immunodeficient (SCID) mouse, it is shown that IgM or IgG positive plasma cells are scattered (left column 2 of page 150 in cited document 2).

Cited documents 3-5 describe that when a human lymphocyte is transplanted to a severe combined immunodeficient (SCID) mouse, a human plasma cell is shown in the mouse.

Cited document 6 describes (1) that a human peripheral blood lymphocyte or a human lung tumor is transplanted to a severe combined immunodeficient (SCID) mouse, (2) that a human Ig is

shown to be produced in the mouse serum due to the transplantation of the human peripheral blood lymphocyte or of the human lung tumor, (3) that it is suggested that a lymphocyte in the tumor is involved in production of the human Ig due to the transplantation of the human lung tumor, and (4) that the growth of a tumor is bad in a cancer in which a human Ig shows a high value and the growth of a tumor is relatively good in a cancer in which a human Ig shows a low value, so the possibility is suggested that the lymphocyte in the tumor is involved also in the growth of an autologous tumor (lines 1-9 of right column of page 491 in cited document 6).

Cited document 7 describes that when a splenic tissue of a stomach cancer patient is transplanted to a severe combined immunodeficient (SCID) mouse and production of a human IgG in the SCID mouse is measured, a high concentration human IgG is produced and that the IgG is considered to be produced in a human plasma cell (Table 1 of page 301 and left column DISCUSSION of page 302 in cited document 7). Furthermore, it is described that using this model allows examination of a monoclonal antibody produced from a human B cell recognizing a tumor cell (lines 32-37 of right column of page 302 in cited document 7).

Claim 1 of the present application is considered to be described in cited documents 1-7.

Claim 2

Claim 2 is described in cited document 6.

Claims 3-33

Cited documents 6 and 7 suggest that an Ig produced from a human plasma cell in an immunodeficient mouse to which a tumor is transplanted or a spleen of a cancer patient is transplanted, recognizes a tumor. So a person skilled in the art could have easily conceived of retrieving a human plasma cell recognizing a tumor from an immunodeficient mouse to which lesions are transplanted, to prepare an antibody against the tumor.

A person skilled in the art could have at that time, as required, performed a fusion with a partner cell, obtained a nucleic acid encoding an antibody from a plasma cell, amplified the nucleic acid encoding the antibody, and chimerized or humanized the antibody, and the like, by applying a well-known technique.

Furthermore, a lung cancer is described in cited document 6 as a kind of a cancer. However, a person skilled in the art could have, as required, performed the same with regard to other cancers. It is not considered especially difficult to employ an obtained antibody as a composition for therapy or diagnosis of lesions, either.

Therefore, a person skilled in the art could have easily arrived at the subject matters of claims 3-33 based on the descriptions of cited documents 6 and 7.

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International application No
PCT/JP2005/007962

Supplemental Box Relating to Sequence Listing

Continuation of Box No. I, item 2:

1. With regard to any nucleotide and/or amino acid sequence disclosed in the international application and necessary to the claimed invention, this report was established on the basis of:

   a. type of material

   ☒ a sequence listing

   ☐ table(s) related to the sequence listing

   b. format of material

   ☐ in written format

   ☒ in computer readable form

   c. time of filing/furnishing

   ☒ contained in the international application as filed

   ☐ filed together with the international application in computer readable form

   ☐ furnished subsequently to this Authority for the purposes of search and/or examination

   ☐ received by this Authority as an amendment [1] on _____

2. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table(s) relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.

3. Additional comments:

[1] *If item 4 in Box No. I applies, the listing and/or table(s) related thereto, which form part of the basis of the report, may be marked "superseded."*